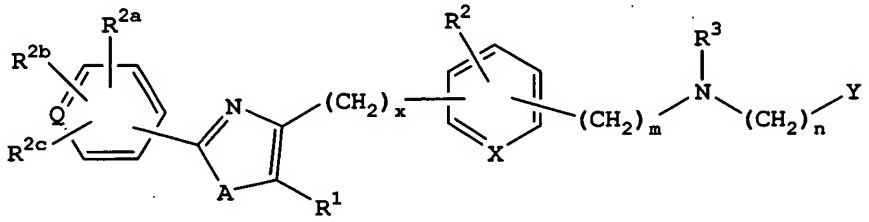
AMENDMENTS TO CLAIMS

Claim 1. (Cancelled).

Claim 2. (Previously Presented) The method as defined in Claim 34 wherein the compound employed has the structure

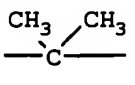
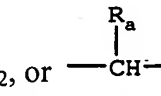


Claims 3 to 4. (Cancelled).

Claim 5. (Previously Presented) The method as defined in Claim 34 where in the compound employed $(CH_2)x$ is alkylene, alkenylene, allenyl, or alkynylene.

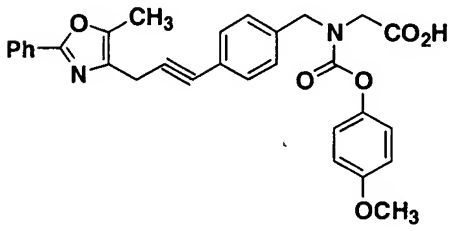
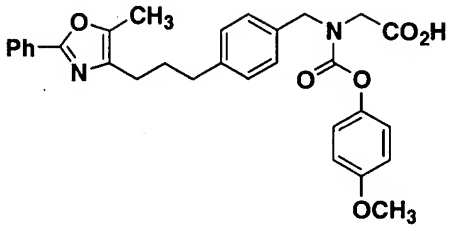
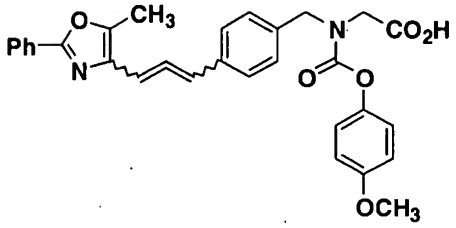
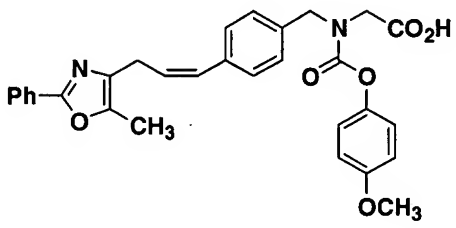
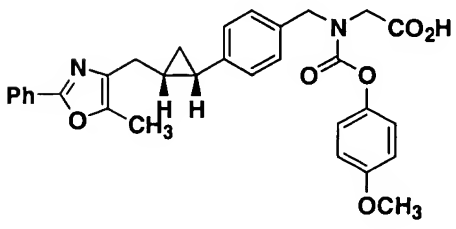
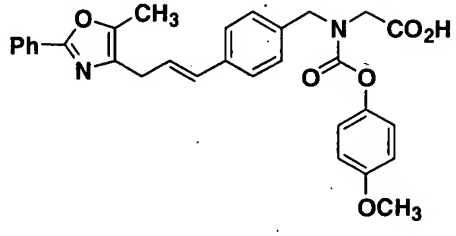
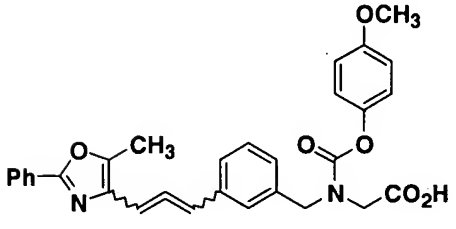
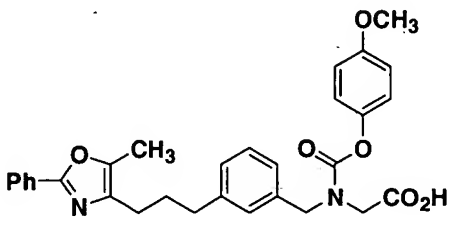
Claims 6 to 9. (Cancelled).

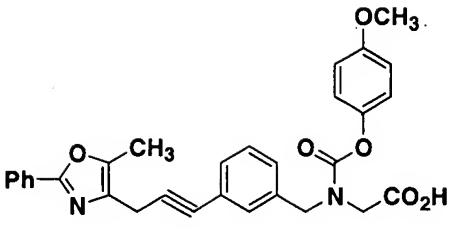
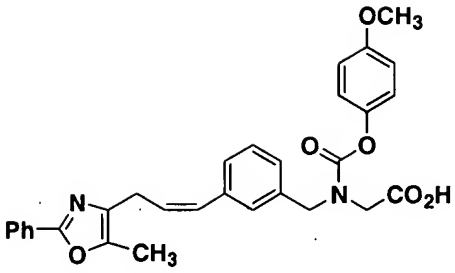
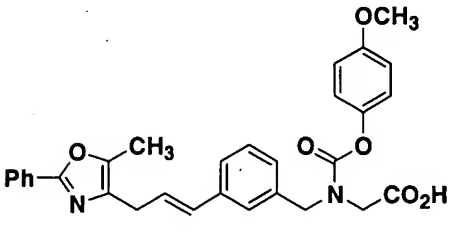
Claim 10. (Previously Presented) The method as defined in Claim 34 where in the compound employed

$(CH_2)_x$ is CH_2, $(CH_2)_2$, $(CH_2)_3$, or  , $(CH_2)_m$ is CH_2, or  where R_a is alkyl or alkenyl, $(CH_2)_n$ is CH_2, R^1 is lower alkyl, R^2 is H, R^{2a} is H, R^4 is H, and R^3 is arylalkyloxycarbonyl, aryloxycarbonyl, haloaryl-oxycarbonyl, alkoxyaryloxycarbonyl, alkylaryloxycarbonyl, aryloxyaryloxycarbonyl, heteroaryloxyarylalkyl, heteroaryloxycarbonyl, arylalkenyloxycarbonyl, cycloalkylaryloxycarbonyl, cycloalkyloxyaryloxycarbonyl, alkyloxyaryloxycarbonyl, arylalkylsulfonyl, arylalkenylsulfonyl, arylthiocarbonyl, cycloheteroalkylalkyloxycarbonyl, cycloheteroalkyloxycarbonyl, or polyhaloalkylaryloxycarbonyl, which may be optionally substituted.

Claims 11 to 15. (Cancelled).

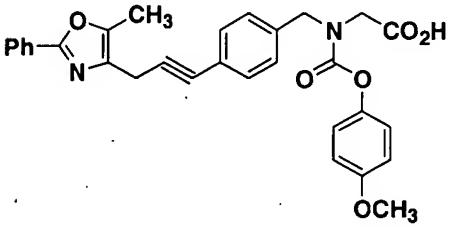
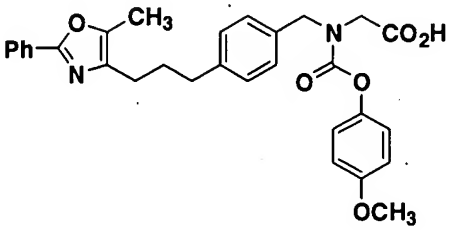
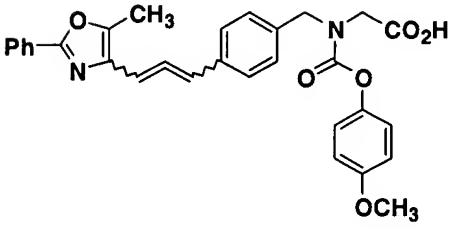
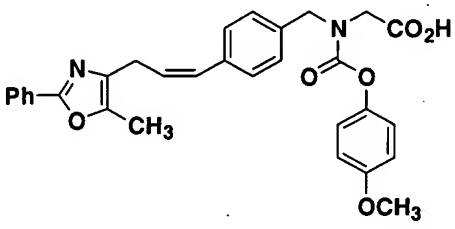
Claim 16. (Currently Amended) The method as defined in Claim 34 wherein the compound employed has the structure

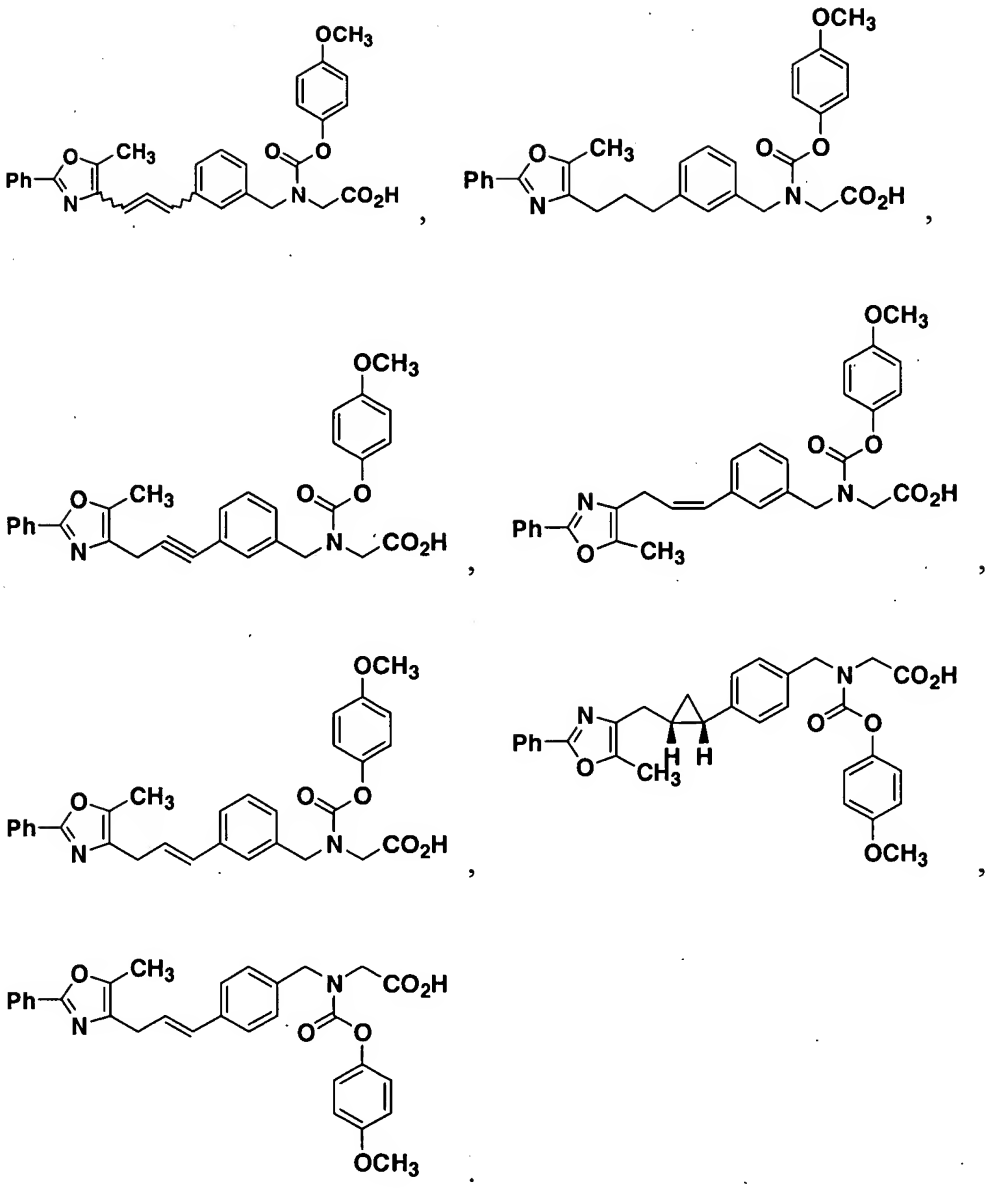

,

,

,

,

,

,

,

,




[[,]] .

Claim 17. (Cancelled).

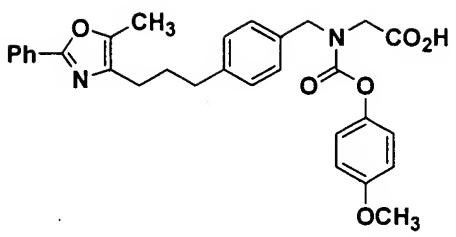
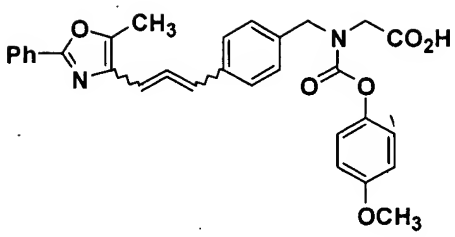
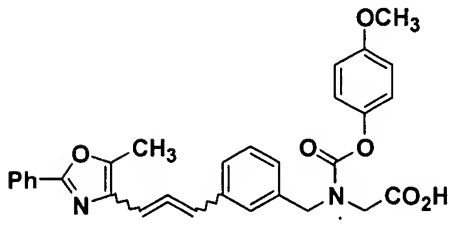
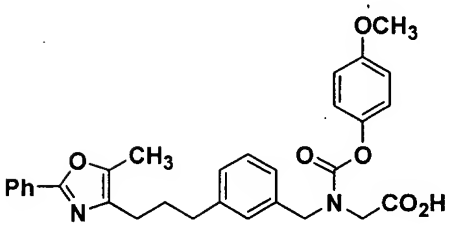
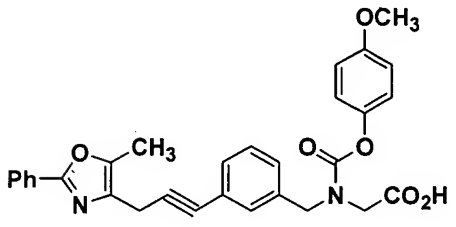
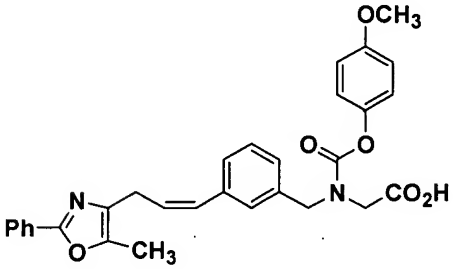
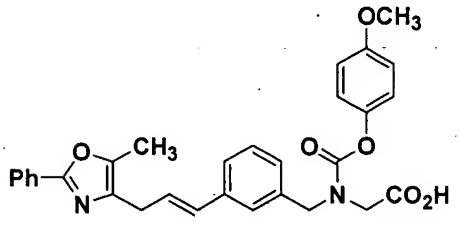
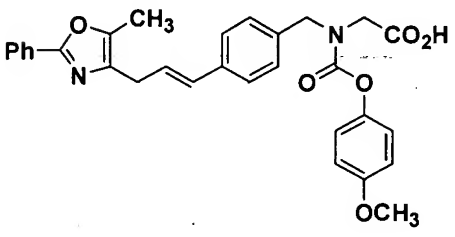
Claim 18. (Previously Presented) The method as defined in Claim 34 wherein the compound employed has the structure



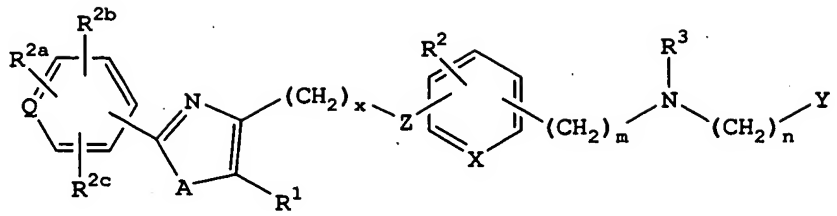
Claim 19. (Cancelled).

Claim 20. (Currently Amended) The method as defined in Claim 34 wherein the compound employed has the structure


,

,

,

,

,

,

,

[[,]].

Claims 21 to 33. (Cancelled).

Claim 34. (Currently Amended) A method for lowering blood glucose levels or for treating diabetes, ~~or for treating an early malignant disease, a malignant disease or a dysplastic disease,~~ which comprises administering to a patient in need of treatment a therapeutically effective amount of a compound which has the structure



wherein x is 1,2, 3 or 4; m is 1 or 2; n is 1 or 2;

Q is C or N;

A is O or S;

Z is O or a bond;

R^1 is H or lower alkyl;

X is CH or N; with the proviso that where Z is O then Q is N or A is S or X is N;

R^2 is H, alkyl, alkoxy, halogen, amino or substituted amino;

R^{2a}, R^{2b} and R^{2c} are the same or different and are selected from H, alkyl, alkoxy, halogen, amino or substituted amino;

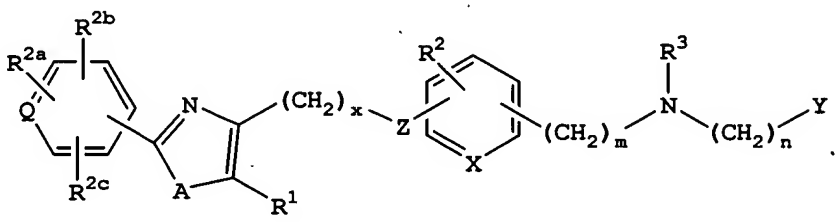
R^3 is aryloxycarbonyl, alkyloxycarbonyl, alkynyloxycarbonyl, alkenyloxycarbonyl, alkyl(halo)aryloxycarbonyl, alkyloxy(halo)aryloxycarbonyl cycloalkylaryloxycarbonyl, cycloalkyloxyaryloxycarbonyl, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, heteroaryloxycarbonylamino, alkylsulfonyl, alkenylsulfonyl, heteroaryloxycarbonyl, cycloheteroalkyloxycarbonyl, heteroarylalkenyl, hydroxyalkyl, alkoxy, alkoxyaryloxycarbonyl, arylalkyloxycarbonyl, alkylaryloxycarbonyl, alkynyloxycarbonyl, haloalkoxyaryloxycarbonyl, alkoxycarbonylaryloxycarbonyl, aryloxyaryloxycarbonyl, arylalkenyloxycarbonyl, heteroaryloxyarylalkyl, aryloxyarylalkyloxycarbonyl, aryloxyalkyloxycarbonyl, arylalkylsulfonyl, arylthiocarbonyl, arylalkenylsulfonyl, heteroarylsulfonyl, arylsulfonyl, heteroarylalkoxycarbonyl, heteroarylalkyloxyarylalkyl, arylalkenylarylalkyl, arylalkoxycarbonylheteroarylalkyl, heteroaryloxyarylalkyl, arylalkenylheteroarylalkyl or polyhaloalkylaryloxycarbonyl;

Y is CO_2R^4 were R^4 is H or alkyl, or a prodrug ester or Y is a C-linked 1-tetrazole, a phosphinic acid of the structure $P(O)(OR^{4a})R^5$ here R^{4a} is H or a prodrug ester, R^5 is alkyl or aryl or a phosphonic acid of the structure $P(O)(OR^{4a})_2$ where R^{4a} is H or a prodrug ester;

or stereoisomers thereof, a prodrug ester thereof, ~~and~~ or a pharmaceutically acceptable salt thereof.

Claims 35 and 36. (Cancelled).

Claim 37. (Currently Amended) A pharmaceutical combination comprising a compound which has the structure



wherein x is 1,2, 3 or 4; m is 1 or 2; n is 1 or 2;

Q is C or N;

A is O or S;

Z is O or a bond;

R^1 is H or lower alkyl;

X is CH or N;

R^2 is H, alkyl, alkoxy, halogen, amino or substituted amino;

R^{2a}, R^{2b} and R^{2c} are the same or different and are selected from H, alkyl, alkoxy, halogen, amino or substituted amino;

R^3 is aryloxycarbonyl, alkyloxycarbonyl, alkynyloxycarbonyl, alkenyloxycarbonyl, alkyl(halo)aryloxycarbonyl, alkyloxy(halo)aryloxycarbonyl cycloalkylaryloxycarbonyl, cycloalkyloxyaryloxycarbonyl, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, heteroaryloxycarbonylamino, alkylsulfonyl, alkenylsulfonyl, heteroaryloxycarbonyl, cycloheteroalkyloxycarbonyl, heteroarylalkenyl, hydroxyalkyl, alkoxy, alkoxyaryloxycarbonyl, arylalkyloxycarbonyl, alkylaryloxycarbonyl, alkynyloxycarbonyl, haloalkoxyaryloxycarbonyl, alkoxycarbonylaryloxycarbonyl, aryloxyaryloxycarbonyl, arylalkenyloxycarbonyl, heteroaryloxyarylalkyl,

aryloxyarylalkyloxycarbonyl, aryloxyalkyloxycarbonyl, arylalkylsulfonyl, arylthiocarbonyl, arylalkenylsulfonyl, heteroarylsulfonyl, arylsulfonyl, heteroarylalkoxycarbonyl, heteroarylalkyloxyarylalkyl, arylalkenylarylalkyl, arylalkoxycarbonylheteroarylalkyl, heteroaryloxyarylalkyl, arylalkenylheteroarylalkyl or polyhaloalkylaryloxycarbonyl;

Y is CO_2R^4 were R^4 is H or alkyl, or a prodrug ester or Y is a C-linked 1-tetrazole, a phosphinic acid of the structure $P(O)(OR^{4a})R^5$ here R^{4a} is H or a prodrug ester, R^5 is alkyl or aryl or a phosphonic acid of the structure $P(O)(OR^{4a})_2$ where R^{4a} is H or a prodrug ester;

or stereoisomers thereof, a prodrug ester thereof, or a pharmaceutically acceptable salt thereof and a lipid-lowering agent, a lipid modulating agent, an antidiabetic agent other than a DP4 inhibitor, an anti-obesity agent other than a DP4 inhibitor, an antihypertensive agent which is other than a diuretic, a platelet aggregation inhibitor, and/or an antiosteoporosis agent.

Claim 38. (Cancelled)

Claim 39. (Previously Presented) The combination as defined in Claim 37 wherein the antidiabetic agent is 1, 2, 3 or more of a biguanide, a sulfonyl urea, a glucosidase inhibitor, a PPARα agonist, a PPAR γ agonist, a PPAR α/γ dual agonist, an SGLT2 inhibitor, a DP4 inhibitor, an aP2 inhibitor, an insulin sensitizer, a glucagon-like peptide-1 (GLP-1), insulin and/or a meglitinide; the anti-obesity agent is a beta 3 adrenergic agonist, a lipase inhibitor, a serotonin (and dopamine) reuptake inhibitor, a thyroid receptor agonist, an aP2 inhibitor and/or an anorectic agent; the lipid lowering agent is an MTP inhibitor, an HMG CoA reductase inhibitor, a squalene synthetase inhibitor, a fibric acid derivative, an upregulator of LDL receptor activity, a lipoxygenase inhibitor, or an ACAT inhibitor; the antihypertensive agent is an ACE inhibitor, angiotensin II receptor antagonist, NEP/ACE inhibitor, calcium channel blocker and/or β-adrenergic blocker.

Claim 40. (Previously Presented) The combination as defined in Claim 39 wherein the antidiabetic agent is 1, 2, 3 or more of metformin, glyburide, glimepiride, glipyride, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, pioglitazone, troglitazone, rosiglitazone, insulin, Gl-262570, isaglitazone, JTT-501, NN-2344, L895645, YM-440, R-119702, AJ9677, repaglinide, nateglinide, KAD1129, AR-HO39242, GW-409544, KRP297, AC2993, LY315902, P32/98 and/or

NVP-DPP-728A; the anti-obesity agent is orlistat, ATL-962, AJ9677, L750355, CP331648, sibutramine, topiramate, axokine, dexamphetamine, phentermine, phenylpropanolamine, and/or mazindol; the lipid lowering agent is pravastatin, lovastatin, simvastatin, atorvastatin, cerivastatin, fluvastatin, itavastatin, visastatin, fenofibrate, gemfibrozil, clofibrate, avasimibe, TS-962, MD-700, cholestagel, niacin and/or LY295427; the antihypertensive agent is an ACE inhibitor which is captopril, fosinopril, enalapril, lisinopril, quinapril, benazepril, fentiapril, ramipril or moexipril; an NEP/ACE inhibitor which is omapatrilat, [S[(R*,R*)]-hexahydro-6-[(2-mercapto-1-oxo-3-phenylpropyl)amino]-2,2-dimethyl-7-oxo-1H-azepine-1-acetic acid (gemopatrilat) or CGS 30440;

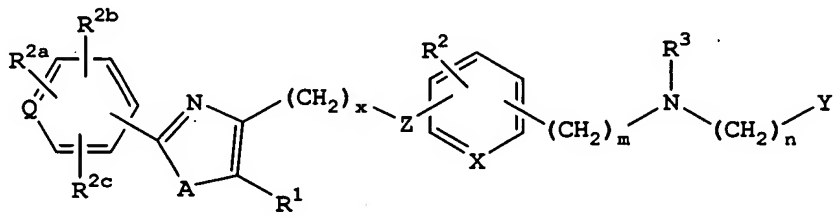
an angiotensin II receptor antagonist which is irbesartan, losartan or valsartan;

amlodipine besylate, prazosin HCl, verapamil, nifedipine, nadolol, propranolol, carvedilol, or clonidine HCl; the platelet aggregation inhibitor is aspirin, clopidogrel, ticlopidine, dipyridamole or ifetroban.

Claims 41 to 49. (Cancelled).

Claim 50. (Previously Presented) A method for treating insulin resistance, hyperglycemia, hyperinsulinemia, or elevated blood levels of free fatty acids or glycerol, hyperlipidemia, obesity, Syndrome X, dysmetabolic syndrome, inflammation, diabetic complications, impaired glucose homeostasis, impaired glucose tolerance, hypertriglyceridemia, atherosclerosis, or for treating irritable bowel syndrome, Crohn's disease, gastric ulceritis or osteroporosis, or psoriasis, which comprises administering to a mammalian species in need of treatment a therapeutically effective amount of a pharmaceutical combination as defined in Claim 37.

Claim 55. (Previously Presented) A pharmaceutical combination comprising a compound which has the structure



wherein x is 1,2, 3 or 4; m is 1 or 2; n is 1 or 2;

Q is C or N;

A is O or S;

Z is O or a bond;

R^1 is H or lower alkyl;

X is CH or N;

R^2 is H, alkyl, alkoxy, halogen, amino or substituted amino;

R^{2a}, R^{2b} and R^{2c} are the same or different and are selected from H, alkyl, alkoxy, halogen, amino or substituted amino;

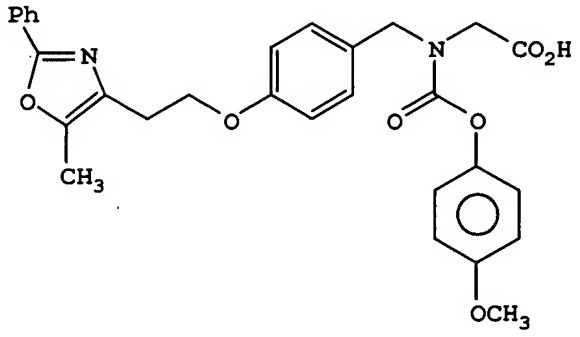
R^3 is aryloxycarbonyl, alkyloxycarbonyl, alkynyloxycarbonyl, alkenyloxycarbonyl, alkyl(halo)aryloxycarbonyl, alkyloxy(halo)aryloxycarbonyl, cycloalkylaryloxycarbonyl, cycloalkyloxyaryloxycarbonyl, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, heteroaryloxycarbonylamino, alkylsulfonyl, alkenylsulfonyl, heteroaryloxycarbonyl, cycloheteroalkyloxycarbonyl, heteroarylalkenyl, hydroxyalkyl, alkoxy, alkoxyaryloxycarbonyl, arylalkyloxycarbonyl, alkylaryloxycarbonyl, alkynyloxycarbonyl, haloalkoxyaryloxycarbonyl, alkoxycarbonylaryloxycarbonyl, aryloxyaryloxycarbonyl, arylalkenyloxycarbonyl, heteroaryloxyarylalkyl, aryloxyarylalkyloxycarbonyl, aryloxyalkyloxycarbonyl, arylalkylsulfonyl, arylthiocarbonyl, arylalkenylsulfonyl, heteroarylsulfonyl, arylsulfonyl, heteroarylalkoxycarbonyl, heteroarylalkyloxyarylalkyl, arylalkenylarylalkyl, arylalkoxycarbonylheteroarylalkyl, heteroaryloxyarylalkyl, arylalkenylheteroarylalkyl or polyhaloalkylaryloxycarbonyl;

Y is CO_2R^4 where R^4 is H or alkyl, or a prodrug ester or Y is a C-linked 1-tetrazole, a phosphinic acid of the structure $P(O)(OR^{4a})R^5$ where R^{4a} is H or a prodrug ester, R^5 is alkyl or aryl or a phosphonic acid of the structure $P(O)(OR^{4a})_2$ where R^{4a} is H or a prodrug ester;

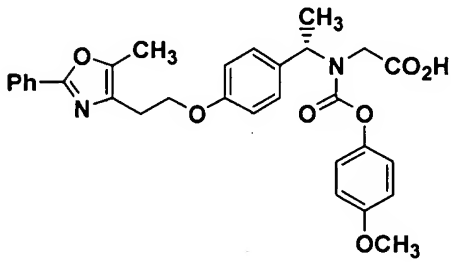
or stereoisomers thereof, a prodrug ester thereof, or a pharmaceutically acceptable salt thereof, and an antihypertensive agent which is a diuretic.

Claim 56. (Previously Presented) The combination as defined in Claim 55 wherein the diuretic is hydrochlorothiazide, torasemide, furosemide, spironolactone or indapamide.

Claim 57. (New) The pharmaceutical combination as defined in Claim 55 wherein the compound has the structure

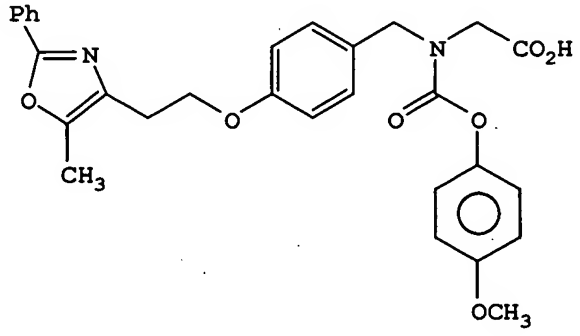


or

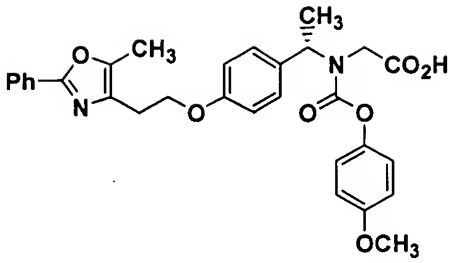


or a pharmaceutically acceptable salt thereof.

Claim 58. (New) A pharmaceutical combination comprising a compound having the structure



or



or a pharmaceutically acceptable salt thereof,
in combination with another therapeutic agent which is metformin or a salt thereof, a sulfonyl urea, SCH 58,235, an HMG CoA reductase inhibitor, a fibric acid derivative, cholestyramine, colestipol, nicotinic acid, acipimox, acifran, or avasamibe.

Claim 59. (New) The combination as defined in Claim 58 wherein the other therapeutic agent is metformin or metformin in the form of its hydrochloride salt.

Claim 60. (New) The combination as defined in Claim 58 wherein the other therapeutic agent is lovastatin, simvastatin, itavastatin, visastatin, atorvastatin, clofibrate, pravastatin, fluvastatin, fenofibrate, benzafibrate, gemfibrizol or probucol.

Claim 61. (New) The combination as defined in Claim 58 wherein the other therapeutic agent is a sulfonyl urea.

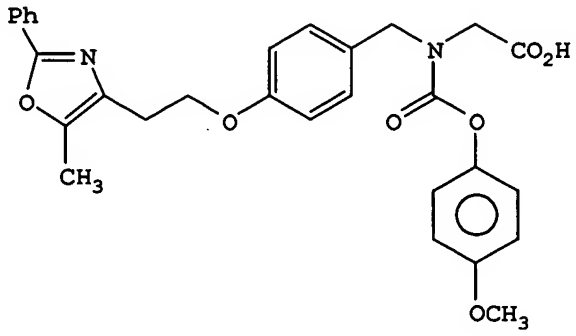
Claim 62. (New) The combination as defined in Claim 61 wherein the sulfonyl urea is glyburide, glimepiride, glipyride, glipizide, or gliclazide.

Claim 63. (New) The combination as defined in Claim 58 wherein the other therapeutic agent is glyburide or glipizide.

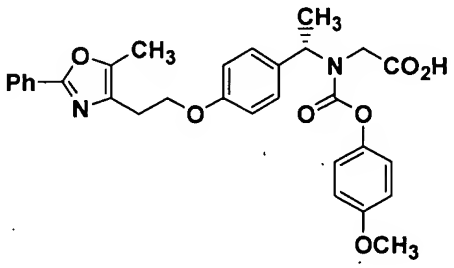
Claim 64. (New) The combination as defined in Claim 57 wherein the other therapeutic agent is atorvastatin.

Claim 65. (New) The combination as defined in Claim 57 wherein the other therapeutic agent is simvastatin or pravastatin.

Claim 66. (New) A pharmaceutical combination comprising a compound having the structure



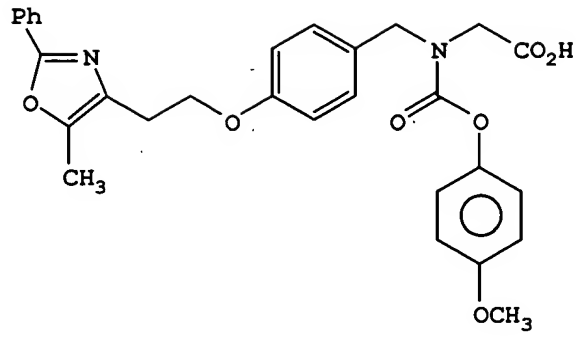
or



or a pharmaceutically acceptable salt thereof,
in combination with another therapeutic agent which is irbesartan or losartan.

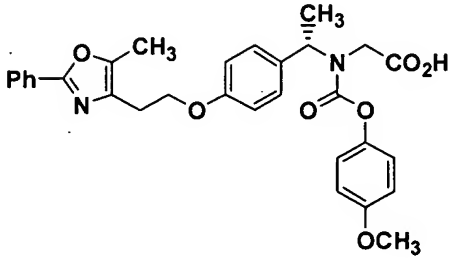
Claim 67. (Previously Presented) The combination as defined in Claim 66 wherein the other therapeutic agent is irbesartan.

Claim 68. (New) A method for lowering blood glucose levels or for treating diabetes, which comprises administering to a patient in need of treatment a therapeutically effective amount of a compound which has the structure



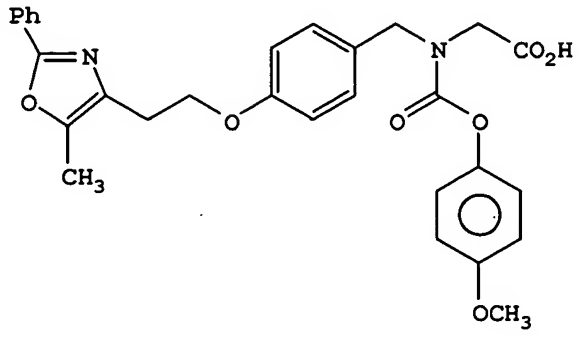
or a pharmaceutically acceptable salt thereof, or

which has the structure

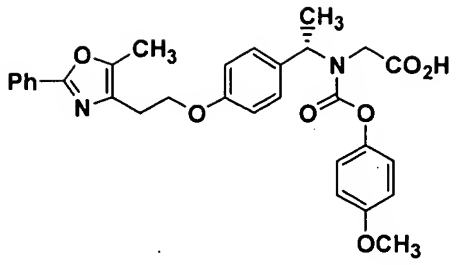


or a pharmaceutically acceptable salt thereof.

Claim 69. (New) A pharmaceutical combination comprising a compound having the structure



or



or a pharmaceutically acceptable salt thereof,

and a DP4 inhibitor.